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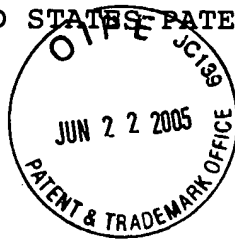
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Richard J. Feldmann

Serial No. 09/866,925

Filed: May 30, 2001



Group Art Unit 1645

Examiner John S. Brusca

For: Algorithmic determination of flanking DNA sequences
that control the expression of sets of genes in
prokaryotic, archea and eukaryotic genomes

APPEAL BRIEF TRANSMITTAL

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Attached hereto are three (3) copies of the BRIEF ON APPEAL for the above-identified application. Also attached is a check which includes \$250.00 (small-entity) in payment of the brief fee as provided by 37 C.F.R. 1.17(f).

A three-month extension of time to extend the period for filing the Brief on Appeal is requested. The fee of \$510.00 is included in the attached check.

Any additional fees necessary to effect the proper and timely filing of this Brief may be charged to Deposit Account No. 26-0090.

Respectfully submitted,

A handwritten signature in cursive script that reads "Jim Zegeer".

Jim Zegeer, Reg. No. 18,957
Attorney for Appellant

Attachments: Brief on Appeal (3 copies)
Check - \$760.00

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801 North Pitt Street
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Date: June 22, 2005

In the event this paper is deemed not timely filed, the applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to Deposit Account No. 26-0090 along with any other additional fees which may be required with respect to this paper.



Atty. Docket No.: 3124-Z

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Richard J. Feldmann

Serial No. 09/866,925

Group Art Unit 1645

Filed: May 30, 2001

Examiner John S. Brusca

For: Algorithmic determination of flanking DNA sequences
that control the expression of sets of genes in
prokaryotic, archea and eukaryotic genomes

BRIEF ON APPEAL

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is an appeal from the final rejection mailed September
23, 2004 of Claims 20 - 37 of the above-identified application.

I. The Real Party in Interest

The real party in interest is Global Determinants, Inc.

II. Related Appeals and Interferences

There are no related appeals or interferences.

III. Status of the Claims

Claims 20 - 37 are pending in the application. Claims 1 - 19
have been cancelled.

IV. Status of the Amendments

There was no amendment filed subsequent to the final rejection.

V. Summary of the Invention

The invention is directed to a computer mediated method of identifying DNA sequences that control the expression of different collections of genes in a genome. DNA sequences of an organism (the genome thereof) are analyzed by computer to identify DNA control sequences, called C1, C2 in the algorithm which meets certain specific criteria set forth at pages 26-36 of the description. Further, identified sequences behave in such a way that when the control sequence (C1 and C2) is transcribed into RNA, the RNA will seek out and bind the target sequences T1 and T2 (C1 binding to T1 and C2 binding to T2) to achieve the effect that the entire DNA sequence beginning with T1 and ending with T2 is shielded from transcription.

VI. Issues

Was the Examiner correct in finally rejecting claims 20 - 37 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and/or use the invention?

VII. Grouping of Claims

The claims do not stand or fall together. Appellant contests the grouping of the claims for reasons which will appear hereinafter in connection with the claims for which the grouping is challenged.

VIII. Argument

The claims stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, the Examiner citing *In re Wands*, 8 USPQ2d 1400 (CAFC 1988).

The claims are all directed to computer mediated methods of genome investigation in which the tetradic relationship between two specific adjacent RNA single-stranded sequences interact with two different double-stranded DNA sequences. Claim 20 refers to a computer algorithm for identifying DNA sequences that control the expression of different collections of genes of a genome comprising detecting by computer one or more pairs of non-adjacent DNA sequences in which are bound one RNA molecule comprising two RNA sequences. *In re Wands* does not deal with computer mediated matters.

In rebuttal to the 35 U.S.C. §112, first paragraph, rejections, appellant submitted two declarations, one of Dr. Richard W. Pastor, and the second of James B. Oberthaler.

Both declarations traverse the Examiner's conclusion that undue experimentation is necessary in order to practice the invention. The Oberthaler¹ declaration concludes:

Finally, in conclusion, I disagree with the Examiner's contention that the trial and error experimentation required to practice the invention amounts to undue experimentation for the following reasons:

(1) As stated earlier, the algorithms presented are straightforward and complete.

(2) No experimentation whatsoever is required. Implementing the algorithms is a routine exercise in program design, coding and debugging. Running them is simply a matter of obtaining the organism-specific genomes and allowing the computer programs to go to work on them.

(3) The only part of the activity that could conceivably be referred to as "experimenting" is the investigation into available bioinformatics resources, such as the syntax and semantics of the resources provided by, for example, that National Library of Medicine's National Center for Biotechnology Information (NCBI). It is clear that in this context, having a ready understanding of this information is a reasonable characteristic of one who could be called "skilled in the art."

(Note: Even *In re Wands* recognized that some experimentation is permissible. 84 USPQ 1400, at p. 1404.)

Dr. Pastor states as follows:

The skilled practitioner would turn to the instant description and drawings for guidance in using the

¹ Mr. Oberthaler has a minority interest (less than 10%) in a licensee of the invention.

claimed invention. The specification provides a detailed roadmap for practicing the invention by one skilled in the art. Referring specifically to the specification and drawings, the introduction at pages 1 - 3 provides a basic description of connectron structure. Figures 1 - 3 are taken from the text by Alberts et al. entitled "The Molecular Biology of the Cell." Pages 3 - 25. Pages 26 - 36 provides a detailed description of a connectron structure. Page 31, the detailed description of the invention, provides a descriptive analysis of the flow diagrams utilized in the computer analysis of connectrons in any given genome. Additionally, ten samples of connectrons found by computer mediation are set out in the specification. Pages 39 - 56 give an example of a prokaryote connectron - E. coli. hence, the algorithm is clearly defined and could be programmed by a skilled scientist. In this sense, the amount of experimentation is quite predictable.

I agree that the nature of the invention, gene control, is complex, and that prior art does not discuss connectron symmetries; i.e., it is my understanding and belief that the connectron invention disclosed in the instant application was made by the inventor, Richard J. Feldmann. [The page references are to the original specification.]

To the extent that *In re Wands* applies to claims dealing with computer mediated genome matters, the Oberthaler and Pastor declarations rebut the Examiner's contention that undue experimentation is necessary in order to practice the invention. Both declarations clearly establish that a detailed roadmap for practicing the invention by one skilled in the art is given in the specification. Both declarations traverse the Examiner's conclusion that undue experimentation is necessary in order to practice computer mediating steps recited in the claims. The Oberthaler declaration establishes that one skilled in the art (a journeyman, molecular biologist, bioinformatician, or computer

programmer who understands the storage format, content and use of readily available bioinformatics resources) can write software following the algorithm that will analyze the DNA sequence of an organism to identify DNA sequences (called C1, C2, T1, T2 in the description of the algorithm) meeting specific criteria set forth in the description. And, further, that the identified sequences behave in such a way that when the control sequence containing C1 and C2 is transcribed into RNA, the RNA will seek out and bind to the target sequence (C1 binding to T1 and T1 and C2 binding to T2 to achieve the effect that the entire DNA sequence beginning with T1 and ending with T2 is shielded from transcription. (See page 4 of the Oberthaler declaration.)

In support of his contention, the Examiner refers to page 29, paragraph 113 of appellant's specification that: "The physical existence and lifetimes of the connectrons must be proved by molecular biological experimentation." This, however, is taken out of context. The full paragraph reads as follows:

The physical existence and lifetimes of the connectrons must be proved by molecular biological experimentation. This physical experimentation process, however, is logically quite separate from the computational experimentation that have been conducted from June of 1999 to May of 2001. The computational search for the existence of connectrons has been extremely positive. These computations have shown that connectrons exist in prokaryotes, in archea, between prokaryotes and their plasmids, in single-celled eukaryotes, in multi-celled eukaryotes, in plants, in higher animals and in humans. All of these features and properties are described in the claims section that follows.

The physical experimentation process is quite separate from the computational experimentation that has been conducted. Appellant respectfully submits that these declarations fully refute the Examiner's contention that claims 20 - 37 contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make or use the invention and that undue experimentation is required.

With respect to the Examiner's contention that the description does not provide working examples of using identified connectron symmetry to predict effects on gene expression (page 3 of Office action), item subparagraph c)), Mr. Oberthaler states:

I disagree. On the contrary, this is exactly what the examples provide. As explained in the introduction and in the definitions provided, (particularly, the definitions of Possible Connectron and Hierarchy of Connectron Action) each connectron control sequence C1-C2 will, when transcribed into RNA, seek out and bind to its target sequence T1-T2, thereby shielding the DNA between T1 and T2 from transcription. Since the shielded DNA sequence will not be transcribed, any genes in the span between T1 and T2 will not be expressed as proteins for as long as the C1-C2 sequence remains bound to T1-T2. Similarly, any additional C1-C2 sequences in the span between T1 and T2 will also remain inactive during this time period, and therefore the inability effect they otherwise would have exerted on their target sequences will be suppressed during this time period. Granted that the full, cascading sequence of transcription/expression and sequestration that would result from each of the examples discussed is not presented, the principles are given that would enable anyone who understands the mechanism, as explained in the application, to follow the effects as deeply as he or she desires.

Claim 21 is directed to a computer mediated method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising, by computer, detecting changes in connectron behavior in a genome as a function of changes in the sequence of the genome.

Claim 22 differs in that this claim is directed to a computer mediated method of detecting changes caused by the application of an exogenous stimulus.

Claim 23 differs in that this claim is directed to a method of detecting by computer where and when new genes have been integrated into a host genome comprising detecting an operable link between a newly introduced gene and a preexisting connectron behavior in the host genome.

Claim 24 is directed to a computer mediated method of detecting the expression effect of different gene collections comprising detecting by computer the effect of connectrons on transcription.

Claim 25 is directed to a method of changing the expression of different gene collections in a genome by identification of connectron organization.

Claim 26 is directed to a method of detecting connectron control and target sequences in a given genome by computer, determining the base composition of the genome, determining one or more sites of control sequence organization, and/or determining one or more sites of target application.

Claim 27 is directed to a computer mediated method of determining the response of a cell in any tissue to changes in the cell's environment and/or genetic composition, by computer, providing a complete genomic DNA sequence for the organism and determining the effect of changes in connectrons due to application of a given exogenous stimulus to the genome.

Claims 28 - 37 are dependent from claim 20 and stand or fall with that claim.

CONCLUSION

In conclusion, appellant submits that Mr. Oberthaler was correct in stating:

The specification provides a detailed roadmap for practicing the invention by one skilled in the art. Referring specifically to the specification and drawings, the introduction at pages 1 - 3 provides a basic description of connectron structure. Figures 1 - 3 are taken from the text by Alberts et al. entitled "The Molecular Biology of the Cell." Pages 3 - 25. Pages 26 - 36 provides a detailed description of a connectron structure. Page 31, the detailed description of the invention, provides a descriptive analysis of the flow diagrams utilized in the computer analysis of connectrons in any given genome.

Ten samples of connectrons found by computer mediation are set out in the specification. Pages 39 - 56 give an example of a prokaryote connectron - E. coli. I have considered this example as well as all examples given against the backdrop of the Examiner's contention that the description lacks clear evidence of the connectron symmetries as related to gene expression and in my opinion that the skilled practitioner would not have any difficulty in practicing the invention from these descriptions for the following reasons:

(1) The flowcharting conventions used are typical of these used to present computer algorithms. Together,

they provide all the detail required for a complete implementation.

(2) A wide variety of computer languages could be used to implement the algorithm. Any procedural third generation language could be used.

(3) These skills are well within the competence of even journeyman programmers using languages such as Fortran, Cobol, PL-I, ALGOL< Pascal. etc, as well as more modern languages such as C, C++, etc.

(4) Computers with the necessary performance and capacity are readily available for an amount that is well within the reach of many home budgets, let alone the resources available to corporations and research institutions.

Appellant respectfully submits that the Examiner erred in finally rejecting claims 20 - 37 and should be reversed.

Respectfully submitted,



Jim Zegeer, Reg. No. 18,957
Attorney for Appellant

Attachment: APPENDIX (Claims on appeal)

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Date: June 22, 2005

In the event this paper is deemed not timely filed, the applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to Deposit Account No. 26-0090 along with any other additional fees which may be required with respect to this paper.

APPENDIX

20. A computer mediated method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising detecting, by computer, one or more pairs of first and second non-adjacent DNA sequences which could bind to one
5 RNA molecule such that a first RNA sequence in that RNA molecule can bind to a first non-adjacent DNA sequence and a second RNA sequence in that RNA molecule can bind to a second non-adjacent DNA sequence.

21. A computer mediated method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising, by computer, detecting, by computer, changes in connectron behavior in the genome as a function of changes in the
5 sequence of the genome.

22. A computer mediated method of detecting changes in expression of different gene collections in a genome, comprising: by computer, detecting changes in expression of different gene collections in a genome that result in changes in the level of connectron control sequences caused by an exogenous stimulus.

23. A computer mediated method of detecting, by computer, where and when new genes have been integrated into a host genome comprising detecting an operable link between a newly introduced gene and a preexisting connectron behavior in said host genome.

24. A computer mediated method of detecting the expression effect of different gene collections in a given host genome, comprising: by computer, detecting the effect of connectrons on transcription.

25. A computer mediated method of changing the expression of different gene collections in a genome comprising modifying, by a computer, identification of connectron organization.

26. A method of detecting connectron control and target sequences in a given genome comprising:

by computer, determining the base composition of said genome, determining one or more sites of control sequence organization, and/or determining one or more sites of target application.

27. A computer mediated method of determining the response of a cell in any tissue to changes in the cell's environment and/or genetic composition comprising: by computer, providing a complete genomic DNA sequence for the organism and determining the effect of changes in connectrons due to application of a given exogenous stimulus to the genome.

28. Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequence and the RNA molecule can form a tetradic relationship such that $T1=C1$ and $T2=C2$ where T1 and T2 are DNA sequences 20 or more bases in length, where the C1 sequence is adjacent to the C2 sequence, where the T1 and T2 sequences are on the same chromosome, and where the C1/C2 sequences are on the same chromosome as T1 and T2 or where the C1/C2 sequences are on a chromosome different from T1 and T2, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

29. Using the method as defined in claim 20, in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a connectron that permits many different C1/C2 short loops to control the existence of a T1-T2 long loop and wherein said C1/C2 short lops can be on the same chromosome or on different chromosomes from the T1-T2 long loop, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

15 C1/C2 - any positive or negative strand DNA sequence of 540 or more bases such that the C1 sequence is adjacent to the C2 sequence,

20 T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

30. Using the method as defined in claim 20, in prokaryotes, archaea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a connectron that permits one C1/C2 short loop to control the existence of many
5 T1-T2 long loops, the C1/C2 short loop can be on the same chromosome or on different chromosomes from the T1-T2 long loops, wherein:

10 C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

15 C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

20 T1 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T2
sequence, the T1 and T2 sequences must be between about 1kb
and 105kb apart, and

25 T2 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T1
sequence, the T2 or T1 sequences must be between about 1kb and
105kb apart.

31. Using the method as defined in claim 20, where the DNA
sequences and the RNA molecule function as a connectron between
prokaryotes and their plasmids and wherein said connectron
implements a control mechanism between the two genomes that makes
5 it possible from them to form a symbiotic relationship, and in the
case of D. radiodurans the relationship is not symmetric, and the
D. radiodurans genome sends C1/C2 short loops to the MP1 plasmid,
wherein:

10 C1 sequence - any positive or negative strand DNA sequence of
20 bases or more, the C2 sequence must occur in the same
chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of
20 bases or more, the C1 sequence must occur in the same
chromosome as the C2 sequence,

15 C1/C2 - any positive or negative strand DNA sequence of 40 or
more bases such that the C1 sequence is adjacent to the C2
sequence,

T1 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T2

20 sequence, the T1 and T2 sequences must be between about 1kb
and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T1
sequence, the T2 or T1 sequences must be between about 1kb and
25 105kb apart.

32. Using the method as defined in claim 20, where the DNA
sequences and the RNA molecule function as a connectron that exist
in a plant or a higher animal.

33. Using the method as defined in claim 20, in prokaryotes,
archaea, single-celled eukaryotes and multi-celled eukaryotes, where
the DNA sequences and the RNA molecule function as a connectron
that permits one C1/C2 short loop to control the existence of one
5 or more T1-T2 long loops without being subject to any expression
controls other than those of the gene to which the C1/C2 is 3'UTR,
wherein:

C1 sequence - any positive or negative strand DNA sequence of
20 bases or more, the C2 sequence must occur in the same
10 chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of
20 bases or more, the C1 sequence must occur in the same
chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or
15 more bases such that the C1 sequence is adjacent to the C2
sequence,

T1 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T2

sequence, the T1 and T2 sequences must be between about 1kb
and 105kb apart,

T2 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T1
sequence, the T2 or T1 sequences must be between about 1kb and
105kb apart, and

3'UTR - untranslated 3' end of an mRNA is beyond the end of
the last exon, a stop codon in the mRNA causes the ribosome to
stop the translation of mRNA into protein.

34. Using the method as defined in claim 20, in prokaryotes,
archaea, single-celled eukaryotes and multi-celled eukaryotes, where
the DNA sequences and the RNA molecule function as a connectron
that permits one C1/C2 short loop to control the existence of one
or more T1-T2 long loops such that this C1/C2 short loop is itself
subject to expression control by another T1-T2 long loop which
surrounds it, wherein:

C1 sequence - any positive or negative strand DNA sequence of
20 bases or more, the C2 sequence must occur in the same
chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of
20 bases or more, the C1 sequence must occur in the same
chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or
more bases such that the C1 sequence is adjacent to the C2
sequence,

T1 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T2

sequence, the T1 and T2 sequences must be between about 1kb
and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T1
sequence, the T2 or T1 sequences must be between about 1kb and
105kb apart.

35. Using the method as defined in claim 20, in prokaryotes,
archaea, single-celled eukaryotes and multi-celled eukaryotes, where
the DNA sequences and the RNA molecule function as a connectron
that permits one C1/C2 short loop to control the existence of the
T1-T2 long loop that surrounds it, wherein:

C1 sequence - any positive or negative strand DNA sequence of
20 bases or more, the C2 sequence must occur in the same
chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of
20 bases or more, the C1 sequence must occur in the same
chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 50 or
more bases such that the C1 sequence is adjacent to the C2
sequence,

T1 sequence - any positive or negative strand DNA sequence of
20bases or more that is on the same chromosome as the T2
sequence, the T1 and T2 sequences must be between about 1kb
and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of
20 bases or more that is on the same chromosome as the T1

sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

36. Using the method as defined in claim 20, where the DNA sequences and the RNA molecule function as a connectron that does not have any genes within the T1-T2 long loop, wherein:

5 T1 sequence is any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, and

10 T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, and the T2 or T1 sequences must be between about 1kb and 105kb apart.

37. Using the method as defined in claim 20, where the DNA sequences and the RNA molecule function as a geneless connectron where one C1/C2 short loop controls the existence of many geneless T1-T2 long loops, wherein:

5 C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

10 C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

15

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

20

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.